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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,974	02/26/2004	Kent Jorgensen	2081-0125P	5458

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1612

NOTIFICATION DATE	DELIVERY MODE
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03/19/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/788,974	Applicant(s) JORGENSEN ET AL.	
	Examiner Gollamudi S. Kishore, Ph.D	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 25-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24, 73 and 74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2-26-04, 8-19-04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-24 and the species wherein X and Z are each O in the reply filed on 6-12-07 is acknowledged. The traversal is on the ground(s) that the group II claims are directed to lipid derivatives per se, but those the same lipid derivatives which are useful in the drug delivery systems and methods of use claimed in Group I... This is not found persuasive because group I is drawn to compositions containing additional ingredients which are not present in Group II. Furthermore, the examiner has already shown the differences in the classification for the compounds and the compositions.

The requirement is still deemed proper and is therefore made FINAL.

Claims included in the prosecution are 1-24 and 73-74.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-24 and 73-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, 'prodrug lipid derivative'; it is unclear as to what the drug is in the composition.

'organic radical' in claim 4 lacks an antecedent basis in claim 1.

Claim 6 which recites the same carbon atoms in R2 is not further limiting the parent claims.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-11, 14-24 and 73-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Hong (4,622,392) or Hong (5,484,911) or Peterson (5,827,836) in combination with Janjic (6,229,002) and Vermehren (BBA, 1998) (the references are all of record).

The references of Hong (392), Hong (911), Peterson each discloses phospholipid prodrugs wherein the carbon 1 of the glycerol has an aliphatic chain and the carbon 2 has an organic radical and carbon 3 has a phosphatidyl group. According to the references, the organic radical is released by phospholipase A2. These phospholipids can be in the form of liposomes (note the abstract, columns 1-6 and Examples of Hong 392; abstract, columns 3-7 and Examples of Hong 911; abstract, columns 7-15 and examples of Peterson).

What is lacking in Hong 392, 911 and Peterson are the teachings of the inclusion of a lipopolymer.

Janjic while disclosing lipid constructs containing PDGF teaches the several advantages of administration of the composition in the form of liposomes and the

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attachment of PEG to the liposomal surface to shield the liposomal complex from blood proteins and thereby enable it to circulate for extended periods in the blood. According to Janjic, the prodrug is on the outside surface of the liposomes (note the abstract, col. 25, line 5 through col. 28, line 67).

Vermehren while disclosing liposomes containing PEG teaches that PEG not only provide steric hindrance which leads to a decrease in the adsorption and interaction of plasma degrading proteins with the liposomal surface, but also enables PLA2 to have increased catalytic activity on the phospholipid containing liposomes. Based on their studies, Vermehren suggest that one can design and optimize the in vivo degradation of drug loaded liposomes at certain sites, e.g., in extra vascular inflammatory tissue due to an enhanced local concentration of the active PLA2 and an accumulation of polymer -grafted liposomes in such tissue (note pages 31-34).

The use of polymer (PEG) containing liposomes for the delivery of the prodrugs of Hong 392, or 911 or Peterson would have been obvious to one of ordinary skill in the art because the advantages of the liposomes and the ability of PEG to prolong the circulation time of the liposomes and increasing their susceptibility to PLA2 in the host pathological tissue and thereby increasing the release of the drug attached to the carbon 2 of the phospholipids.

6. Claims 12-13 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Hong (4,622,392) or Hong (5,484,911) or Peterson (5,827,836) in combination with Janjic (6,229,002) and Vermehren (BBA, 1998) as set forth above, further in view of Saxon (Journal of Liposome Research, 1999) or Bally (5,736,155).

The teachings of Hong 392 and 911, Peterson, Janjic and Vermehren have been discussed above. What is lacking in Hong, Peterson, Janjic and Vernerren is the administration of the composition with an additional liposome encapsulated drug.

Saxon teaches that anticancer drugs can be used in combination in liposomes (summary).

Bally similarly teaches the encapsulation of two anticancer drugs in liposomes (col. 15, Part C).

The use of an additional liposomal anticancer agent would have been obvious to one of ordinary skill in the art, with the expectation of obtaining an additional effect, since the references of Saxon and Bally show that two anticancer drugs can be used in combination.

7. Claims 1-11, 14-24 and 73-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozak (6,166,089) of record in combination with Janjic (6,229,002) and Vermehren (BBA, 1998) of record.

Kozak discloses phospholipid prodrugs wherein the carbon 1 of the glycerol has an aliphatic chain and the carbon 2 has an organic radical and carbon 3 has a phosphatidyl group. According to Kozak the organic radical is released by phospholipase A2 present in the pathological tissue (note the abstract, col. 4, line 41 through col. 11, line 9, Examples and claims).

What are lacking in Kozak are the inclusion of a lipopolymer and the administration of the composition in the form of liposomes.

Janjic while disclosing lipid constructs containing PDGF teaches the several advantages of administration of the composition in the form of liposomes and the attachment of PEG to the liposomal surface to shield the liposomal complex from blood proteins and thereby enable it to circulate for extended periods in the blood. According to Janjic, the prodrug is on the outside surface of the liposomes (note the abstract, col. 25, line 5 through col. 28, line 67).

Vermehren while disclosing liposomes containing PEG teaches that PEG not only provide steric hindrance which leads to a decrease in the adsorption and interaction of plasma degrading proteins with the liposomal surface, but also enables PLA2 to have increased catalytic activity on the phospholipid containing liposomes. Based on their studies, Vermehren suggest that one can design and optimize the in vivo degradation of drug loaded liposomes at certain sites, e.g., in extra vascular inflammatory tissue due to an enhanced local concentration of the active PLA2 and an accumulation of polymer -grafted liposomes in such tissue (note pages 31-34).

The use of polymer (PEG) containing liposomes for the delivery of the prodrug of Kozak would have been obvious to one of ordinary skill in the art because the advantages of the liposomes and the ability of PEG to prolong the circulation time of the liposomes and increasing their susceptibility to PLA2 in the host pathological tissue and thereby increasing the release of the drug attached to the carbon 2 of the phospholipid in Kozak.

8. Claims 12-13 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozak (6,166,089) of record in combination with Janjic (6,229,002) and

Vermehren (BBA, 1998) as set forth above, further in view of Saxon (Journal of Liposome Research, 1999) or Bally (5,736,155).

The teachings of Kozak, Janjic and Vermehren have been discussed above. What is lacking in Kozak, Janjic and Vernerren is the administration of the composition with an additional liposome encapsulated drug.

Saxon teaches that anticancer drugs can be used in combination in liposomes (summary).

Bally similarly teaches the encapsulation of two anticancer drugs in liposomes (col. 15, Part C).

The use of an additional liposomal anticancer agent would have been obvious to one of ordinary skill in the art, with the expectation of obtaining an additional effect, since the references of Saxon and Bally show that two anticancer drugs can be used in combination.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

GSK

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